UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,320	07/21/2005	Per Mansson	Mans3011/REF	3650

23364 7590 06/28/2006

BACON & THOMAS, PLLC
625 SLATERS LANE
FOURTH FLOOR
ALEXANDRIA, VA 22314

EXAMINER	
JUNG, UNSU	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 06/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/517,320	MANSSON ET AL.	
	Examiner	Art Unit	
	Unsu Jung	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *8-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 November 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/20/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' amendment to claim 1 in the reply filed on April 13, 2006 has been acknowledged and entered.

2. Claims 1-12 are pending.

Election/Restrictions

3. Applicant's election with traverse of Group I (claims 1-7) in the reply filed on April 13, 2006 is acknowledged. The traversal is on the ground(s) that the U.S. Patent No. 6,699,665 does not teach "low molecular weight antigens bound via the amide-group to the SAM-forming OEG molecule." This argument is persuasive as the U.S. Patent No. 6,699,665 does not teach "low molecular weight antigens bound via the amide-group to the SAM-forming OEG molecule. However, Willner et al. (WO 00/43774, July 27, 2000) in view of Svedhem et al. (*J. Org. Chem.* 2001, Vol. 66, pp4494-4503) and Bentley et al. (U.S. PG Pub. No. US 2001/0027212 A1, Oct. 4, 2001) teaches a self-assembled monolayer (SAM) of oligo(ethylene glycol)-terminated (OEG-terminated) alkanethiol amides on gold coated surface on a solid support having low molecular weight antigens bound via an amide group to the SAM-forming OEG molecules and antibodies reversibly bound to antibodies specific for the antigens as discussed below. Therefore prior art teaches the special technical feature of Groups I-IV.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

4. The information disclosure statement filed on November 20, 2004 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the references, which have been lined through, have not been considered.

Drawings

5. The drawings are objected to because vertically written "TNT" should be changed to "TNT100" on bottom right graph of Fig. 9. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as

either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

6. The use of the trademark MILLIQ™ (p8, lines 4, 5, and 18) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claim 1 lacks a transitional phrase such as “comprising”, “consisting of”, and “consisting essentially of”, which define the scope of a claim with respect to what unrecited additional components, if any, are excluded from the scope of the claim. See MPEP 2111.03. Therefore, claim 1 is vague and indefinite as it is unclear as to what is being claimed and metes and bounds of the claimed invention is not clearly defined. For the purpose of examination, claim 1 has been interpreted as being inclusive or open-ended and does not exclude additional, unrecited elements.

10. Claim 1 recites the limitation "the coating" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.
The term "low molecular weight" in claim 1 is a relative term which renders the claim indefinite. The term "low molecular weight " is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The limitation of “low molecular weight antigens” has been rendered indefinite by the use of the term “low molecular weight.”

11. In claim 1, the term “an amide-group” in line 4 is vague and indefinite. It is unclear whether or not the term “an amide-group” in line 4 is referring to “an amide group” in line 2. For the purpose of examination, the term “an amide-group” in line 4 has been interpreted as being different from an amide group” in line 2.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 1, 2, 6, and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Willner et al. (WO 00/43774, July 27, 2000) in view of Svedhem et al. (*J. Org. Chem.* 2001, Vol. 66, pp4494-4503) and Bentley et al. (U.S. PG Pub. No. US 2001/0027212 A1, Oct. 4, 2001).

Willner et al. teaches a sensitive method of detecting small amount of low molecular weight compounds (typically below about 1,500 Daltons), which includes explosive molecules such as DNT and TNT and drugs such as heroin and cocaine (p5, lines 1-15) using quartz crystal microbalance (QCM). Willner et al. further teaches that any method intended for sensing the presence of explosive molecules or other types of low molecular weight molecules such as drugs should be highly sensitive and adapted for detecting a small amount of molecules. The QCM includes a piezoelectric crystal sandwiched between two gold electrodes (Abstract and p23, lines 14-17) coated with an antigen, which is then contacted with an antibody (p24, lines 8-12). Measurement of resonance frequency at this stage yields a certain basic frequency (p24, lines 9-12). Challenging the electrode with a sample comprising antigens causes release of some of the antibodies to yield a soluble antigen-antibody complex, which reduces the immobilized mass and consequently the frequency is increased as a result of and signifies the presence of the assayed molecule in the medium (p24, lines 13-19). However, Willner et al. fails to teach a coated metal surface further comprising a self-assembled monolayer (SAM) of oligo(ethylene glycol)-terminated (OEG-terminated) alkanethiol amides.

Svedhem et al. teaches a self-assembled monolayer (SAM) of oligo(ethylene glycol)-terminated (OEG-terminated) alkanethiol amides on gold coated surface on a solid support (p4503, right column, *Preparation of SAMs*) designed to address structure and stability of biosensing interfaces (Abstract). SAM-forming OEG molecules includes alkyl portion of the alkanethiols having 2, 5, 11, and 15 CH_2 groups (methylene groups) and OEG portion has 1, 2, 4, 6, 8, 10, and 12 (CH_2CH_2O) (ethylene oxy) units (Abstract). Organic modifications of gold surfaces by SAMs have proven to be successful in biosensor applications (p4494, *Introduction*, second paragraph). Furthermore, ethylene glycols provide good anchors for biological receptors and ligands and reduce nonspecific binding of proteins and other bioactive molecules (p4494, *Introduction*, first paragraph). Poly(ethylene glycol) derivatives are also ideal as spacer candidates because they are inexpensive, water soluble, stable, and available in a wide range of molecular weight distributions (p4494, *Introduction*, first paragraph). However, Svedhem et al. fails to teach low molecular weight antigens bound via an amide group to the SAM-forming OEG molecules.

Bentley et al. teaches that conventional amide linkages formed between amine groups on drugs, which include peptides, proteins and small agents (antigens), having amine groups and PEG through non-hydrolyzable amide linkages, which are generally stable (p1, paragraph [0007]). However, Bentley et al. fails to teach that antigens are reversibly bound to antibodies specific for the antigens.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ SAM of OEG-terminated alkanethiol amides of Svedhem

et al. in the QCM biosensor of Willner et al. in order to provide a biosensing interface with structurally stable SAM, which reduce nonspecific binding of proteins and other bioactive molecules. The advantage of having a structurally stable SAM, which has the characteristic of reducing nonspecific binding of proteins and other bioactive molecules provides the motivation to include the SAM of OEG-terminated alkanethiol amides of Svedhem et al. in the QCM biosensor of Willner et al. with a reasonable expectation of success since the solid support of Willner et al. includes a gold coated surface and Svedhem et al. teaches that he SAM of OEG-terminated alkanethiol amides can be formed on gold coated surfaces for use as a biosensing interfaces. Furthermore, it would have been obvious to one of ordinary skill in the art at the time of the invention to use conventional amide linkages formed between amine groups on drugs and ethylene glycol of OEG as taught by Bentley et al. in order to immobilize antigens of interest on the SAM of OEG-terminated alkanethiol amides of Svedhem et al. as the amide linkages are generally stable and non-hydrolyzable. The advantage of amide linkages, which are stable and non-hydrolyzable provides the motivation to employ amide linkages to immobilize antigens of Willner et al. on the SAM of OEG-terminated alkanethiol amides of Svedhem et al. with a reasonable expectation of success as Bentley et al. teaches that small molecules such as drugs can be immobilized to ethylene glycols of PEG, which are also present in OEGs.

16. Claims 3-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Willner et al. (WO 00/43774, July 27, 2000) in view of Svedhem et al. (*J. Org. Chem.*

2001, Vol. 66, pp4494-4503) and Bentley et al. (U.S. PG Pub. No. US 2001/0027212 A1, Oct. 4, 2001) as applied to claim 1 above, and further in view of Duffy (U.S. PG Pub. No. US 2002/0028463 A1, Mar. 7, 2002).

Willner et al. in view of Svedhem et al. and Bentley et al. teaches a coated metal surface on a solid support as discussed above. Willner et al. further teaches that antigens are selected from a group consisting of explosives and narcotics (p5, lines 1-15). However, Willner et al. in view of Svedhem et al. and Bentley et al. fails to teach a coated metal surface on a solid support, wherein the antigens are bound to the same or different monolayers in patches on the solid support.

Duffy teaches an array system which can be used to elucidate interactions between molecules (p5, paragraph [0039]). The system comprises array of binding areas (patches) for immobilizing biomolecules and provides for high throughput, as many interactions may be tested in a single assay (p5, paragraphs [0040] and [0041]). Duffy further teaches that the interactions between molecules can be detected using QCM (p13, paragraph [0113]).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include an array of binding patches for immobilization of antigens of the Willner et al. in view of Svedhem et al. and Bentley et al. as taught by Duffy in order to perform high throughput analysis of many interactions, which may be tested in a single assay. The advantage of having the capacity to perform high throughput analysis of many interactions, which may be tested in a single assay, provides the motivation to include an array of binding patches for immobilization of

antigens of the Willner et al. in view of Svedhem et al. and Bentley et al. with a reasonable expectation of success since Duffy teaches that the array system can be used with QCM detection methods to detect binding interaction on the array surface.

With respect to claim 4, Willner et al. teaches derivatized explosives, which include trinitrotoluene (TNT) and dinitrotoluene (DNT, Fig's 1A and 1B). The derivatized DNT includes an amine group, which form an amide linkage with ethylene glycol of OEG.

With respect to claim 5, Willner et al. teaches antigens are selected from cocaine and heroine (p5, lines 13-15).

Conclusion

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Unsu Jung whose telephone number is 571-272-8506. The examiner can normally be reached on M-F: 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Unsu Jung, Ph.D.
Patent Examiner
Art Unit 1641

LONG V. LE 06/28/06
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600